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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/511,691	10/14/2004	David Hands	20974YP	9304

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RAHWAY, NJ 07065-0907

EXAMINER

ANDERSON, REBECCA L

ART UNIT	PAPER NUMBER
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1626

MAIL DATE	DELIVERY MODE
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05/21/2007

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/511,691	Applicant(s) HANDS ET AL.	
	Examiner Rebecca L. Anderson	Art Unit 1626	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on ____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 is/are pending in the application.
- 4a) Of the above claim(s) ____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) ____ is/are allowed.
- 6) ☒ Claim(s) 1-14 is/are rejected.
- 7) ☐ Claim(s) ____ is/are objected to.
- 8) ☐ Claim(s) ____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on ____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. ____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|---|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. ____. |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date <u>10/14/2004</u> . | 6) <input type="checkbox"/> Other: ____. |

DETAILED ACTION

Claims 1-14 are currently pending in the instant application and are rejected.

Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1, 10, 13 and 14 are rejected under 35 U.S.C. 102(b) as being anticipated by US Patent No. 5,719,147.

US Patent No. 5,719,147 discloses the stereochemistry of the compound corresponding to applicants' formula 1 on column 45, lines 45-60, which corresponds to the stereochemistry found in applicants' claims 13 and 14. This compound is prepared in example 75, column 104 from 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenyl morpholine (which corresponds to applicants formula 2) by the method of example 70, column 102 wherein 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenyl-4-(2-(N-methylcarboxyacetamidrazono)morpholine (which corresponds to applicants formula 4) in 15ml of xylenes was heated at reflux for 2 hours. Heated at reflux in xylenes corresponds to applicants temperature of 140-150 degrees Celsius as can be seen in the CRC Handbook of Chemistry and Physics wherein the boiling points of the xylene solvents are 138, 139 and 144 degrees Celsius. US Patent NO. 5,719,147 discloses drying prior to cyclization wherein in example 70, lines 18 and 19 state that the organic layer was separated, dried over magnesium sulfate and concentrated in vacuo.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-14 are rejected under 35 U.S.C. 103(a) as being unpatentable over US Patent No. 5,719,147.

Determining the scope and contents of the prior art

US Patent No. 5,719,147 discloses substituted heterocycles of the structure as found on column 5 and their methods of preparation, columns 53-67. US Patent No. 5,719,147 discloses the stereochemistry of the compound corresponding to applicants' formula 1 on column 45, lines 45-60, which corresponds to the stereochemistry found in applicants' claims 13 and 14. This compound is prepared in example 75, column 104 from 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenyl morpholine (which corresponds to applicants formula 2) by the method of example 70, column 102 wherein 2(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenyl morpholine is reacted with N-methylcarboxy-2-chloroacetamidrazone and N,N-diisopropylethylamine in acetonitrile at room temperature for 20 hours. The organic layer was separated, dried over magnesium sulfate and concentrated in vacuo. Then 2-(R)-(1-(R)-(3,5-bis(trifluoromethyl)phenyl)ethoxy)-3-(S)-(4-fluoro)phenyl-4-(2-(N-methylcarboxyacetamidrazono)morpholine (which corresponds to applicants formula 4) in 15ml of xylenes was heated at reflux for 2 hours. Heated at reflux in xylenes corresponds to applicants temperature of 140-150 degrees Celsius as can be seen in the CRC Handbook of Chemistry and Physics wherein the boiling points of the xylene solvents are 138, 139 and 144 degrees Celsius.

Ascertaining the differences between the prior art and the claims at issue

The difference between the prior art and the claims at issue is that the prior art may differ: in the temperature of the cyclization; by not using the hydrochloride salt of the compound of formula 2 and toluene; by using diisopropylethylamine as the inorganic

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base instead of sodium carbonate, cesium carbonate, sodium hydroxide, potassium hydroxide and potassium carbonate; by using acetonitrile as a polar aprotic solvent instead of dimethylformamide, dimethylsulfoxide; or by not washing with an aqueous phase such as KCl, KHCO₃, K₂CO₃, Na₂CO₃, NaHCO₃ and NaCl.

Resolving the level of ordinary skill in the pertinent art

However, it would have been obvious to one of ordinary skill in the art at the time of the invention, when faced with the prior art of US Patent No. 5,719,147, to prepare the compound of formula 1 as claimed as the prior art provides the cyclization of the compound of formula 4 in xylenes at reflux since the boiling point of xylenes are 138, 139 and 144. One would be motivated by the expectation of additional methods to prepare compounds of the formula 1 by utilizing xylene which has a boiling point of 144 degrees Celsius or modifying the temperature from 138 and 139 degrees Celsius as the optimization of variables in a known process is prima facie obvious. It would have been obvious to one of ordinary skill in the art to use toluene and the HCl salt of the formula 2 when faced with the prior art reference as the prior art reference provides in another process of preparing substituted heterocycles of the structure as found on column 5, the use of an HCl salt and toluene, see example 101, column 131 wherein the hydrochloride salt of the product was broken by slurrying in a mixture of toluene and sodium bicarbonate. It would have been obvious to use an inorganic base other than diisopropylethylamine as the prior art reference provides the use of appropriate bases to include diisopropylethylamine, potassium carbonate, sodium carbonate and the like on column 66 and utilizes the inorganic base of potassium carbonate in example 83,

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column 107 with the polar aprotic solvent of DMF as the optimization of variables in a known process is prima facie obvious. Additionally, it would have been obvious to use a polar aprotic solvent other than acetonitrile, such as DMF as the prior art reference provides the use of both of these polar aprotic solvents in the preparation of the substituted heterocycles of the structure as found on column 5, see example 83. Lastly, the washing of the compound of the formula 4 with an aqueous phase, such as KCl would have been obvious as the prior art provides washing with sodium bicarbonate in example 101, column 131 and the optimization of variables in a known process is prima facie obvious.

Conclusion

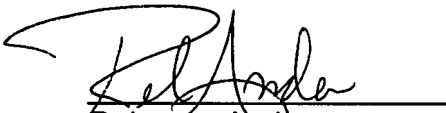
Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Rebecca L. Anderson whose telephone number is (571) 272-0696. Mrs. Anderson can normally be reached Monday through Friday 5:30AM to 2:00PM.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Mr. Joseph K. McKane, can be reached at (571) 272-0699.

The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



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17 May 2007